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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,938	CHORY ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *24 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☒ Claim(s) *25 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/3/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-27 are pending.

2. Applicant's election with traverse of Group I, claims 1-23, 25-26, including SEQ ID NO:2 encoding SEQ ID NO:7 filed 12/4/2003 is acknowledged. The traversal is on the ground(s) that if a search and examination of an application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to distinct or independent inventions". Applicants respectfully submit that the claimed nucleic acid sequences e.g., SEQ ID NOs: 1, 2, 3, and 9), and their corresponding amino acid sequences (SEQ ID NOs: 6, 7, 8 and 10) are so structurally related that they can be examined together without imposing a serious burden on the Examiner (page 5, 3rd paragraph). Applicants contend that there is 99% sequence identity between SEQ ID NO:1 and 2 and between the corresponding amino acid sequences of SEQ ID NO:6 and 7. In addition, there is also a 99% sequence identity between SEQ ID NO:3 and 9 and between the corresponding amino acid sequences of SEQ ID NO:8 and 10. Applicants contend that there is an 88% sequence identity between SEQ ID NO:6 and 8 and that because of the high degree of identity, it would not be an undue burden on the examiner to search all the sequences together. The Applicants also contend that it has been determined that normally up to ten sequences constitute a reasonable number for examination purposes.

This is not found persuasive because SEQ ID NO:6 and 8 only exhibit 88% sequence identity to each other and a search of one sequence will not adequately cover a search of the other sequence, especially in light of Applicants claims drawn to a nucleic acid sequence encoding an amino acid sequence with at least 80% sequence homology. In addition, while the search of the prior art for one group may overlap with that of another, they are not co-extensive

of each other and thus would be a burden on the Office. In regards to the permissible number of sequences as specified in the MPEP, those guidelines were for EST sequences which are much shorter than the nucleic acid sequences presented in the present application, and because of the vast number of sequences now present in the current databases that must be searched, the office does not have the resources to search more than one corresponding pair of nucleic acid and amino acid sequences per application. And lastly, according to the MPEP, up to ten sequences will be examined, and one sequence is considered up to ten, for the reasons stated above.

SEQ ID NO:1 encoding SEQ ID NO:6 is rejoined and will be examined in the present office action.

The requirement is still deemed proper and is therefore made FINAL.

Claims 24 and 27 have been withdrawn from consideration because the claims are drawn to non-elected inventions.

3. Claims 1-23, 25-26, including SEQ ID NO:1 and 2 encoding SEQ ID NO:6 and 7 are examined in the present office action.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See for example page 36, line 12. See MPEP § 608.01.

Claim Objections

5. Claims 6, 7, 13, 14, 22, and 23 are objected to for reading on non-elected inventions. Correction is required.

Claims 9-11, line 1, are objected to for omitting the word "sequence" after the recitation "amino acid".

Claims 9-11, line 2, are objected to for reciting "comprises" instead of "exhibits".

Claim 13, lines 1 and 2, is objected to for reciting "amino acid" instead of "polypeptide".

Claims 18-20, line 1, are objected to for omitting the word "sequence" after the recitation "amino acid".

Claims 18-20, line 2, are objected to for reciting "comprises" instead of "exhibits".

Claim 22, lines 1 and 2, is objected to for reciting "amino acid" instead of "polypeptide".

Claims 25 and 26, line 1, are objected to for omitting the word "molecule" after the recitation "nucleic acid".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 8-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

In claims 8 and 17, it is recommended that the word "homology" be replaced with

--identity--. The meaning of the word "homology" is indefinite as it is not clear how relatedness is determined, whether by sequence relatedness alone, by evolutionary relatedness, or by some other means.

In claims 9-11 and 18-20, it is recommended that the word "homology" be replaced with --sequence identity--. The meaning of the word "homology" is indefinite as it is not clear how relatedness is determined, whether by sequence relatedness alone, by evolutionary relatedness, or by some other means.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 8-12, and 15-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of producing a genetically modified plant comprising a nucleic acid sequence encoding any brassinazole resistant polypeptide, a genetically modified plant or seed comprising a nucleic acid sequence encoding any brassinazole resistant polypeptide wherein said polypeptide comprises an amino acid sequence exhibiting at least 80%, 85%, 90% or 95% homology or sequence identity to SEQ ID NO:6.

Applicants disclose the BRASSINAZOLE RESISTANT 1 (BRZ1) and BRZ2 encoding nucleic acids of SEQ ID NO:1 and 3 encoding the corresponding amino acid sequences of SEQ ID NO:6 and 8.

Applicants do not identify essential regions of the BRZ1 protein encoded by SEQ ID NO:1 nor do Applicants disclose nucleic acid sequences from other species of plants that encode a polypeptide exhibiting 80% sequence identity to SEQ ID NO:6 and encode a BRZ1 polypeptide with the same function as the polypeptide of SEQ ID NO:6. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences from more than one plant species encoding a BRZ1 protein falling within the scope of the claimed genus of polynucleotides which encode a polypeptide that exhibits at least 80% sequence identity to SEQ ID NO:6 or 7 . Applicants only describe two wild-type Arabidopsis sequences of SEQ ID NO:1

and 3 encoding SEQ ID NO:6 and 8. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the BRZ1 protein, it remains unclear what features identify an Arabidopsis BRZ1 protein. Since the genus of BRZ1 proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Sequences that encode polypeptides exhibiting at least 80% sequence identity or homology to SEQ ID NO:6 or 7 encompass naturally occurring allelic variants, mutants of BRZ1 protein, as well as sequences encoding proteins having no known BRZ1 activity, of which Applicant is not in possession. Absent of such disclosure, one skilled in the art cannot determine the genus of sequences based upon the disclosure of the sequence of SEQ ID NO:1 or 2 encoding SEQ ID NO:6 or 7 with any certainty or predictability. Accordingly, the specification fails to provide an adequate written description to support the percent identity or homology language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Scope of Enablement

8. Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule comprising a nucleotide sequence encoding a bzr1-D polypeptide of SEQ ID NO:7, a nucleic acid molecule of SEQ ID NO:2, a method of producing a genetically modified plant having increased size as compared to a wild-type plant, a

genetically modified plant exhibiting increased size in comparison to a wild-type plant, or a genetically modified seed that produces a plant with increased size in comparison to a wild-type plant comprising transforming a plant with a nucleic acid encoding SEQ ID NO:7 or wherein the nucleic acid sequence is set forth in SEQ ID NO:2, does not reasonably provide enablement for claims drawn to a method of producing a genetically modified plant having increased size compared to a wild-type plant, a genetically modified plant exhibiting increased size in comparison to a wild-type plant, or a genetically modified seed that produces a plant with increased size in comparison to a wild-type plant comprising transforming a plant with a nucleic acid encoding any brassinazole resistant polypeptide, a brassinazole resistant polypeptide comprising an amino acid sequence exhibiting at least 80%, 85%, 90% or 95% sequence identity or homology to SEQ ID NO:6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to a method of producing a genetically modified plant having increased size, comprising any brassinazole resistant polypeptide transformed therewith, a genetically modified plant exhibiting increased size in comparison to a wild-type plant comprising a nucleic acid sequence encoding a brassinazole resistant polypepetide comprising an amino acid sequence exhibiting at least 80%, 85%, 90%, or 95% sequence identity or homology to SEQ ID NO:6 operably linked to a promoter or genetically modified seed transformed therewith.

Applicants disclose the isolation of the bzr1-D nucleic acid sequence of SEQ ID NO:2 encoding SEQ ID NO:7 using an EMS mutagenesis screen comprising the use of brassinazole, a triazole-type brassinosteroid biosynthesis inhibitor (pages 33 and 34, Examples 2 and 3). Applicants report that over-expression of the brz1-D nucleic acid caused plants to exhibit increased cell elongation which created plants exhibiting long hypocotyls, long petioles, long stems, bigger siliques and larger leaves (pages 37 and 38, Example 8 and Table 2).

Applicants do not teach nucleic acid molecules encoding any brassinazole resistant polypeptide or polypeptides that exhibit at least 80%, 85%, 90%, or 95% sequence identity or homology to SEQ ID NO:6 and transformation of any plants with any such molecules. In addition, Applicants disclose that transforming Arabidopsis with nucleic acids encoding the BRZ1 or BRZ2 polypeptides of SEQ ID NO:6 or 8 did not produce plants with increased cell lengths. Applicants own admitted statements state that "Expression of wild type BZR1 and BZR2 genes from their own promoters did not cause obvious phenotypes" and Table 2 reports "No effect" for plants transformed with 35S:BZR1 or 35S:BZR2 (page 37 and 38, Example 8 and Table 2). Applicants do not teach how to use a plant transformed with BZR1 or BZR2.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that encode polypeptides exhibiting at least 80%, 85%, 90% or 95% sequence identity to SEQ ID NO:6 will encode a protein with the same activity as SEQ ID NO:6. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph). In the present application, a change of the amino acid proline to a leucine at position 231 changes the activity of the protein (page 35, 2nd paragraph).

The state-of-the-art of isolating or synthesizing nucleic acid molecules that encode a polypeptide of defined function is highly unpredictable. Applicants do not teach which amino acids of SEQ ID NO:6 can be deleted or substituted and still produce a protein with the same activity as the protein whose amino acid sequence is set forth in SEQ ID NO:6. Applicants also do not teach which amino acids can be substituted to produce a polypeptide having the activity of the polypeptide whose sequence is set forth in SEQ ID NO:7.

In view of the lack of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences,

either by using non-disclosed fragments of SEQ ID NO:1 as probes or by designing primers to undisclosed regions of SEQ ID NO:1 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, and then to evaluate each plant for a desirable phenotype or characteristic.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, and the lack of teachings by the Applicant as to how one skilled in the art uses a plant transformed with SEQ ID NO:1, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled throughout the full scope of the claims.

9. Claims 1-23 and 25-26 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a method of producing a genetically modified plant having increased size as compared to a wild-type plant, a genetically modified plant exhibiting increased size or a genetically modified seed producing a plant with increased size in comparison to a wild-type plant comprising a nucleic acid sequence encoding a brassinazole resistant polypeptide exhibiting at least 80%, 85%, 90%, or 95% sequence identity to SEQ ID NO:6, or an isolated polynucleotide encoding a bzr1-D polypeptide having the amino acid sequence of SEQ ID NO:7 or wherein the nucleic acid sequence comprises the nucleotide sequence of SEQ ID NO:2.

Allowable Subject Matter

10. Claims 25 and 26 are objected to but would be allowable if rewritten to over-come the objections as stated above.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
February 2, 2004